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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,809	02/02/2005	Koji Kawai	TIP-04-1339	9964

35811 7590 05/29/2008

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,809	KAWAI ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/7/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-12, 14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Attachment(s) 6). Other: Drawings of the compound of formula 1 .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/7/08 has been entered.

The response filed **3/7/08** presents remarks and arguments to the office action mailed **9/7/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of claims

Claims 1-10 are cancelled.

Claims 11-12, 14 and 16 are pending.

Maintained Claim Rejections - 35 USC § 103

Applicant argues that: the Portoghese does not teach a method for treating nausea and vomiting.

That the reference teaches if a ligand acts at a single opioid receptor type or subtype , the potential side effects mediated can be potentially minimized. That the compounds of the instant application are not opioid agonist which cannot induce analgesia, but can treat vomiting. Next Applicant submits' evidence that all side effects induced by morphine cannot always be treated.

Also, that mu-opioid agonist such as morphine show both of directly-opposed effects on emesis in the low range and on the other hand reduces emesis in the high dose.

Applicant further argued by explaining that nicotine is used to cause emesis and not fentamyl. And that there is no incentive to combine.

In response, it is not clear what Applicant is arguing with regards to a ligand acts at a single opioid receptor type or subtype , the potential side effects mediated can be potentially minimized. The claims simply call for treating nausea caused by a mu-opioid agonist. The claims did not call for a ligand acting at a single opioid receptor. Minimizing the potential side effect does not teach the side effects are eliminated completely, minimizing can be instead of maybe having emesis five times in an hour to 1 time. The effect is still present.

With regards to the compounds of the instant application are not opioid agonist, a compound with the same chemical structure, can be named whatever by one of ordinary skill in the art, what does not change is the characteristics of the compound.

With regard to mu-opioid agonist such as morphine show both of directly-opposed effects on emesis in the low range and on the other hand reduces emesis in the high dose, there is no indication what that dosage is by reading the claims. Whether the effective dosage amount is low or high is not taught by the claims. Applicant is reading what is not claimed.

As to the argument that nicotine is used to induce emesis, Examiner agrees but Applicant has not shown that fentamyl do not cause emesis. Infact it is known that fentamyl causes emesis. See as evident by Sosis underlining page, Can. Anasth Soc. J, 1985, 32 (3) 2 pages. Examiner's understanding is that nicotine is given to accelerate emesis characteristics of fentamyl.

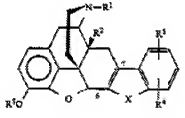
As to the outlined of teachings by Rudd as depicted, careful consideration has been given,where It is *prima facie* obviousness to select a known material based on its suitability for its intended use. *See Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945). Also, established precedent holds that it is generally obvious to add known ingredients to known compositions with the expectation of obtaining their known function. See, e.g., *In re Linder*, 457 F.2d 506, 507 (CCPA 1972); see also *In re Dial*, 326 F.2d 430, 432 (CCPA 1964).

The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior

art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

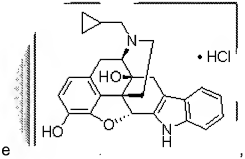
Careful consideration has been given to the arguments and literature Hepburn et al. for Examiners, convenience but found not persuasive. The rejection is maintained.

Claims 11-12, 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Portoghese et al. US 5, 352,680 (of record) taken with of Rudd et al. Europ. J. Pharm. (of record) in view of Neeleman, European Society of Anesthesiologists (newly applied) as evident by Meijer et al., Brain Research, Vol. 868(1) 2000 135-140 **Abstract only**.

Portoghese et al. teach a compound that is structurally identical to that of the claimed compound as  (see col. 14, lines 10 +) as in claims 11 and 12, where R^1 is an alkyl group having 1-5 carbon atoms, R^{2-4} are hydrogen, or R^4 and R^5 together form an O, (as in claim 14) R^6 is hydrogen and Q is

(see col. 14 lines 10-30).

The reference teaches the adverse effect of morphine (as required by instant claim 16, see col. 1, lines 15-24, wherein one such effect is vomiting. if a ligand acts at a single opioid receptor type or subtype, the potential side effects mediated through other opioid receptor types can potentially be minimized or eliminated, thus treating nausea and vomiting (see col. 1, lines 34-43) and the μ-opiod agonist compound is a morphine (see col. 9 lines 8-17). Portoghese et al. teach the compound is an opiod antagonist and belongs to a group of morphinan derivatives. The reference, however, do not specifically identify morphine as a mu-opiod agonist.

Rudd et al. teach naltrindole 

, having the same structure (see enclosed attached structures) to inhibit the emetic reflex (vomiting) (see abstract and also page 82 (section 4.3 first para.) as in claims 20-22. Also note that the anti-emetic action of fentany is antagonized by the opioid receptor antagonist naltrexone. The reference is use to show that the drug has been used to treat vomiting, therefore one of ordinary skill in the art would be motivated to use the drug by Rudd to treat vomiting caused by a mu-opiod agonist. Fentanyl is a mu-opiod agonist see abstract as evident by Meijer et al., Brain Research.

Neeleman teaches Morphine, is a mu-opioid receptor agonist, see underling page 2. One of ordinary skill in the art would know that the properties of a compound

would not change as stated in the MPEP 2112.01"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658
(Fed. Cir. 1990). "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not."

One of ordinary skill in the art would have been motivated to administer the above compounds to a patient wherein the nausea and vomiting is caused by the administration of a mu-opiod agonist (morphine) because the art teaches that naltrindole has been used to specifically inhibit adverse effects of morphine. One of ordinary skill in the art would have been motivated to use the drug, to inhibit vomiting. Therefore one of ordinary skill in the art would have been motivated to administer the drug since the compound as taught has the property of reducing vomiting/nausea as a whole, and would expect the drug to work since the action of is blocking of the stimulation of the emesis zone as it was found to be a member of the morphinan that prevents emetics.

It would therefore have been prima facie obvious to the skilled artisan at the time the invention was made to administer the drug for the treatment of nausea or vomiting as indicated by the above cited prior art.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
5/16/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614